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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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AKZO NOBEL PHARMA PATENT DEPARTMENT
PO BOX 318
MILLSBORO, DE 19966

EXAMINER	
CHEN, STACY BROWN	
ART UNIT	PAPER NUMBER
1648	

DATE MAILED: 04/27/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/749,907	ANTOINETTE VAN DE ZANDE ET AL.	
	Examiner	Art Unit	
	Stacy B. Chen	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03 March 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-20* is/are pending in the application.

4a) Of the above claim(s) *17-20* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-16* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's election without traverse of Group I, claims 1-16, in the reply filed on March 3, 2005 is acknowledged. Claims 1-20 are pending. Claims 17-20 are withdrawn from consideration, being drawn to a non-elected invention. Claims 1-16 are under examination.

Claim Objections

2. Claim 7 is objected to for reciting the acronym, "IFT" and not providing a complete spelling at its first occurrence, as in claim 8, for example.

Claim Rejections - 35 USC § 112

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 2, 7 and 8 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

It is apparent that antibodies INT 13-06, 14-11, 15-01, Reovirus strains ERS 1037, ERS 060E and ERS 074, and strains S1133, 2408, 1733 and 2177 are required to practice the claimed invention because they are a necessary limitation for the success of the invention as stated in the claims. As a required element it must be known and readily available to the public or obtainable by a repeatable method set forth in the specification, or otherwise readily available to the public.

The specification discloses that deposits of antibodies INT 13-06, 14-11, 15-01, Reovirus strains ERS 1037, ERS 060E and ERS 074, and strains S1133, 2408, 1733 and 2177 have been made. However, when a deposit is made under the terms of the Budapest Treaty, then an affidavit or declaration by applicants or someone associated with the patent owner who is in a position to make such assurances, or a statement by an attorney of record over his or her signature, stating that the deposit has been made under the terms of the Budapest Treaty and that all restrictions imposed by the depositor on the availability to the public of the deposited material will be irrevocably removed upon the granting of a patent, would satisfy the deposit requirements. See 37 CFR 1.808.

If a deposit is not made under the terms of the Budapest Treaty, then an affidavit or declaration by applicants or someone associated with the patent owner who is in a position to make such assurances, or a statement by an attorney of record over his or her signature, stating that the deposit has been made at an acceptable depository and that the following criteria have been met:

(a) during the pendency of this application, access to the invention will be afforded to one determined by the Commissioner to be entitled thereto;

(b) all restrictions imposed by the depositor on the availability to the public of the deposited material will be irrevocably removed upon granting of the patent;

(c) the deposit will be maintained for a term of at least thirty (30) years and at least five (5) years after the most recent request for the furnishing of a sample of the deposited material;

(d) a viability statement in accordance with the provisions of 37 CFR 1.807; and

(e) the deposit will be replaced should it become necessary due to inviability, contamination or loss of capability to function in the manner described in the specification.

In addition the identifying information set forth in 37 CFR 1.809(d) should be added to the specification. See 37 CFR 1.803 - 37 CFR 1.809 for additional explanation of these requirements.

4. Claims 1 and 3-16 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of propagating ERS 1037, ERS 060E and ERS 074 in Vero cells without prior adaptation, does not reasonably provide enablement for a method of propagating any avian Reovirus without prior adaptation to Vero cells. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with these claims. The factors considered when determining if the disclosure satisfies the enablement requirement and whether any necessary experimentation is undue include, but are not limited to: 1) nature of the invention, 2) state of the prior art, 3) relative skill of those in the art, 4) level of predictability in the art, 5) existence of working examples, 6) breadth of claims, 7) amount of direction or guidance by the inventor, and 8) quantity of experimentation needed to make or use the invention. *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988). The claims encompass an unreasonable number of inoperative viruses for the claimed method, which the skilled artisan would not know how to use. The nature of the invention is the propagation of wild-type avian reoviruses that are able to grow to a particular titer on Vero cells without prior adaptation to the cell line. The state of the art demonstrates that not all avian reoviruses are capable of growing on Vero cells without prior adaptation. Drastini *et al.* (*J. Virol. Methods*, 1992, 39:269-278, "Drastini") discloses 14 avian reoviruses that were adapted to replicate in Vero cells (abstract).

Drastini also discloses avian reoviruses can grow readily on avian cells, however, the only mammalian cells that supports avian reoviruses is the Vero cell line, which requires adaptation (page 270, first full paragraph). Nwajei *et al.* (*Avian Pathology*, 1988, 17 :759-766, herein, "Nwajei") discloses 22 strains of avian reoviruses that had to be adapted (page 760, *Materials and Methods* section). Nwajei also teaches that Vero cells are unsuitable for the isolation of avian reoviruses from field material (abstract). There are no working examples for avian reoviruses other than ERS 1037, ERS 060E and ERS 074. There is no guidance for using other avian reoviruses than those disclosed and deposited. The skill of those in the art is high, and the level of predictability in the art for propagating avian reoviruses in Vero cells without adaptation is low. It would require undue experimentation to discover other avian reoviruses that have the capability to be propagated to a certain titer in Vero cells. Given the breadth of the claims, the state of the art, the lack of guidance and working examples in the specification and the low level of predictability in the art, the full scope of the claimed invention is not enabled.

5. Claims 1 and 3-16 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The claims are drawn to a method of propagating avian reovirus that are isolated from poultry and grown to suitable titer on Vero cells, without prior adaptation, comprising the steps of inoculating a Vero cell line with the avian reovirus, allowing the reovirus to multiply, and harvesting the avian reovirus. The claims encompass embodiments that are not adequately

described, namely, avian reoviruses isolated from the wild, that do not require adaptation to a Vero cell line and produce particular titers.

To provide adequate written description and evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of complete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, or any combination thereof. The claims only recite a generic avian reovirus (encompassing all wild-type avian reoviruses) and a function (able to grow on Vero cells to a particular titer). *Vas-Cath Inc. v. Mahurkar*, 19USPQ2d 1111, clearly states "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See *Vas-Cath* at page 1116). As discussed above, the skilled artisan cannot envision the all of the wild-type avian reoviruses that can grow on Vero cells without prior adaptation. Not all avian reoviruses are able to grow on Vero cells without prior adaptation, and Applicant's examples (ERS 1037, 060E and 074) do not represent the genus that is claimed. Drastini *et al.* (*J. Virol. Methods*, 1992, 39:269-278, "Drastini") discloses 14 avian reoviruses that were adapted to replicate in Vero cells (abstract). Drastini also discloses avian reoviruses can grow readily on avian cells, however, the only mammalian cells that supports avian reoviruses is the Vero cell line, which requires adaptation (page 270, first full paragraph). Applicant's disclosure reveals certain cell lines isolated from the wild that are capable of growing on Vero cells without

adaptation to the cell line. However, the claims encompass embodiments that were not in possession at the time of Applicant's invention. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The compound itself is required. See *Fiers v. Revel*, 25 USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016.

6. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-16 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

- Claim 1 and dependent claims 2 and 7-16 recite, "grow to suitable titer". The term "suitable" is relative and subject to individual interpretation. Thus, the metes and bounds of the claims are not definite, lacking a clear definition in the specification.
- Claim 3 depends from claim 3, which is not clear. In the interests of compact prosecution, claim 3 will be interpreted to be dependent from claim 1. (Claims 4-6 will be interpreted as dependent from claim 3, as recited). Correction is required.
- Claims 7 and 8 recite limitations of reactivity in an immuno-fluorescence technique with various monoclonal antibodies and polyclonal antiserums. These limitations do not clearly define the metes and bounds of the claims because absence/presence of reactivity is subject to individual interpretation. For example, does the absence of reactivity mean that the antibodies do not bind to the virus at all, or that some antibodies bind, but not

enough for a signal. Defining a virus by the absence of a particular activity (absence of reactivity with various monoclonal antibodies) is not clear. Defining a virus by reactivity with polyclonal antibodies that are reactive with various reoviruses is also unclear. There is no direct correlation between the reoviruses (S113, etc.) and the claimed reoviruses. Correction is required.

- Claims 9-12 recite method step(s) that do not correlate with the preamble of independent claim 1. Claims 9-12 require further steps of using the product that is made, which is unclear because the method of claim 1 is drawn to a method of producing virus. Steps of harvesting and purification, for example, are acceptable additional steps that correlate with a method of production. However, steps of using the product are intended uses, not correlated with a method of production.

Claim Rejections - 35 USC § 102

7. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 8-10, 12, 13 and 16 are rejected under 35 U.S.C. 102(b) as being anticipated by Rekik *et al.* (*Avian Diseases*, 1992, 36:237-246, "Rekik"). The claims are drawn to a method of propagating avian reovirus isolated from poultry and grown to suitable titer on Vero cells, without prior adaptation, comprising the steps of inoculating a Vero cell line with the avian reovirus, allowing the reovirus to multiply, and harvesting the avian reovirus. The reovirus is

characterized by reactivity in an immuno-fluorescence technique with a polyclonal antiserum raised against a reovirus, such as strain S1133. The claimed method produces a Reovirus, which is used for administered to a subject in combination with a pharmaceutically acceptable carrier or diluent. (The Office notes that the limitation of claim 9 is an intended use, which is not given patentable weight.) The reovirus is naturally non-pathogenic and is isolated from a chicken.

Rekik discloses eight avian reovirus isolates from broiler chickens that are grown on monolayers of Vero cells, incubated, harvested, killed. Rekik does not disclose the amount of virus that was harvested from the Vero cell cultures, however, since the specification does not define the "suitable titer" of reoviruses, Rekik's method meets the limitation (page 238, column 1, first full paragraph). Additionally, Rekik's S1133 reovirus preparation would be expected to react with polyclonal serum raised against S1133. Reovirus S1133 is a vaccine strain and used in poultry. The poultry vaccine is expected to contain a pharmaceutically acceptable carrier or diluent. The virus preparation itself contains pharmaceutically acceptable carrier or diluent, buffer (page 238, first column, last paragraph). Regarding the limitation of the reovirus being naturally non-pathogenic, Rekik's reoviruses are not pathogenic to humans. Therefore, the claims are anticipated by Rekik.

Claim Rejections - 35 USC § 103

8. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1, 3-6, 8-10, 12-16 are rejected under 35 U.S.C. 103(a) as being unpatentable over Rekik as applied to claims 1, 8-10, 12, 13 and 16 above, and further in view of Ashmead *et al.* (US 5,162,369, "Ashmead") and Rosenberger *et al.* (US 5,525,342, "Rosenberger"). The claims are drawn to a method of propagating avian reovirus that is isolated from poultry and grown to suitable titer on Vero cells, without prior adaptation, comprising the steps of inoculating a Vero cell line with the avian reovirus, allowing the reovirus to multiply, and harvesting the avian reovirus. The titer of virus is at least 3.0, 4.0, 5.1 and 5.3 $TCID_{50}$/ml. The reovirus is characterized by reactivity in an immuno-fluorescence technique with a polyclonal antiserum raised against a reovirus, such as strain S1133. The reovirus is administered to a subject in combination with another pathogen, such as Infectious Bursal Disease virus (IBDV) with a pharmaceutically acceptable carrier or diluent. The Reovirus is isolated from the brain, spinal chord, and/or other structures associated with the neurological system. The reovirus is naturally non-pathogenic and is isolated from a chicken.

The teachings of Rekik are summarized above. Rekik is silent on the isolation of Reovirus from the brain, spinal chord, and/or other structures associated with the neurological system. Rekik is silent on a combination vaccine with other avian pathogens.

With regard to the limitation of the reovirus being isolated from the neurological system, specifically the brain, spinal chord and/or other structures associated with the nervous system, Reovirus is known to be located in those areas. Ashmead teaches that malabsorption syndrome of warm-blooded mammals is associated with reoviruses, adenoviruses and toga-like particles. Reoviruses have been isolated from various sources such as the pancreas, liver, intestines, spinal cord and femoral bone marrow of birds with malabsorption syndrome (column 14, lines 1-13.)

Ashmead also discloses that most of the Reovirus stocks from birds are serologically correlated to S1133. It would have been obvious to one of ordinary skill in the art at the time of the invention to isolate reoviruses from birds' central nervous system. One would have been motivated to isolate reoviruses from components of the nervous system because it is known to reside there, as taught by Ashmead. One would have had a reasonable expectation of success because Ashmead teaches that reoviruses have been isolated from the spinal cord.

Regarding the claimed method step of using the Reovirus in combination with additional antigenic component, the Office notes that this limitation is an intended use of the product produced by the method of claim 1. As it is an intended use, the limitation does not have patentable weight. However, in order to address every limitation, Rosenberger discloses inactivated combination vaccines of non-pathogenic reovirus 2177 and various avian viruses, such as Marek's disease virus, Newcastle disease virus, IBDV, Infectious bronchitis virus, avian encephalomyelitis virus, fowl pox virus and chicken anemia agent (Rosenberger, claims 1-17). One would have been motivated to make a combination vaccine because one would vaccinate against multiple pathogens simultaneously, as taught by Rosenberger. One would have had a reasonable expectation of success that a combination vaccine would have been successful to simultaneously immunize several pathogens because combination vaccines are well known and applied, evidenced by Rosenberger.

Regarding the various titers of Reovirus produced, the claims do not specify period of time of culturing to obtain the titers. One of ordinary skill would have been able to produce their desired titer. Nonetheless, at the time of the invention, one of ordinary skill would have been capable of optimizing Rekik's method to obtain various titers. Rosenberger discloses

vaccination with approximately 5.0 log base 10 $TCID_{50}$/ml, which meets the titer limitations of claims 3-7 (at least *about* 5.3 $TCID_{50}$/ml). See Example VII, for example.

Therefore, the invention as would have been *prima facie* obvious to one of ordinary skill in the art at the time of the instant invention. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Conclusion

9. No claim is allowed. The subject matter of claim 2, Reovirus strains ERS 1037, 060E and 074 are free of the prior art of record.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Stacy B. Chen whose telephone number is 571-272-0896. The examiner can normally be reached on M-F (7:00-4:30). If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James C. Housel can be reached on 571-272-0902. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Stacy B. Chen

Stacy B. Chen
April 26, 2005